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CASE REPORT

# "Mucinemia": Report of a Case of Carcinomatosis with a Unique Serum Protein

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THIS report concerns a patient with carcinomatosis in whom a peculiar serum protein was found. As no reference to a similar type of serum protein could be found in the literature, it was felt that the case was worthy of recording.

A 72-year-old farm labourer was transferred to Deer Lodge Veterans Hospital, Winnipeg, in September 1960 because of an enlarged liver and the presence of a homogeneous density in a radiograph of his chest.

In 1916, he received a gunshot wound to the right hip and he had been treated on numerous occasions for symptoms referable to that injury. This man had a chronic cough and dyspnea which had been attributed to obstructive pulmonary emphysema and chronic pulmonary sepsis. He had had numerous hospital admissions for these conditions in the past.

In October 1958, he exhibited the classical clinical picture of myocardial infarction, which was confirmed by electrocardiogram. Thereafter he complained of angina on effort.

In September 1960, he was admitted to another hospital because of a two-week history of tarry stools, cough and dyspnea. He was transferred to Deer Lodge Hospital for investigation of an enlarged liver and a circumscribed radiographic density in the left lower lung field that had not been present on a film taken in July 1959.

On admission, the chest findings were consistent with those of chronic pulmonary emphysema. An enlarged, coarsely nodular liver was palpable, the lower margin of which extended to the iliac crest in the axillary line. Radiological investigation of his gastrointestinal tract did not demonstrate any lesion, but his stools were consistently positive for occult blood. Bronchoscopic examination did not give evidence of a specific lesion, and bronchial washings did not contain any tumour cells. A biopsy of the liver disclosed the presence of a metastatic adenocarcinoma.

On admission, the following laboratory data were recorded: the hemoglobin was 8.2 g. %, erythrocyte count 2.7 million per c.mm., and hematocrit 25%. The examination of a blood film disclosed hypochromia, anisocytosis, microcytosis and numerous pencil cells consistent with an iron-deficiency anemia due to chronic blood loss. Prothrombin estimation was 60% of normal; bromsulphalein excretion showed 60% retention after half an hour. The serum alkaline phosphatase was 20.8 King-Armstrong units. His total serum bilirubin was 0.88 mg. %, and the direct-reacting bilirubin was 0.15 mg. %. The thymol turbidity was 1.5 MacFarlane units, and the cephalin cholesterol flocculation 1+ in 24 hours. Urinalysis showed a trace of protein and occasional pus and red cells. Electrophoretic analysis of the serum proteins revealed a total protein of 5.90 g. %, albumin 2.52 g., alpha$_1$ globulin 0.56 g., alpha$_2$ globulin 0.47 g., beta globulin 0.54 g. and a gamma globulin of 1.81 g. %.

The clinical diagnosis was adenocarcinoma; the probable primary site, the lung, with extensive metastases in the liver. His general course was downhill. He developed progressive jaundice, emaciation, lethargy and anorexia, and died on October 28, 1960.

*Autopsy*

The essential findings in an examination performed 12 hours post mortem were as follows. The liver was enlarged, weighing 5600 grams, and occupied most of the abdominal cavity. Its external surface was studded with nodules; many were budding above the liver surface and many were hemorrhagic and necrotic in appearance. Sections of six of these nodules all showed a papillary mucus-secreting adenocarcinoma. The tumour was composed of moderately pleomorphic, tall columnar cells with hyperchromatic nuclei and a delicate fibrous stroma. Periodic acid-Schiff stain showed the presence of abundant mucus in the tumour cells.

In the stomach a shallow ulcer 2.5 cm. in diameter was found on the greater curvature 2 cm. from the cardia. It was irregular in outline, circular, poorly demarcated and with a rough, hard, granular base. The tumour extended to the serosal surface, and histologically it showed involvement of small and large venous and lymphatic channels. Its microscopic appearance was much the same as that of the metastatic nodules in the liver.

The lungs were involved by marked emphysematous changes with bulla formation and bronchiectasis. A hard, sharply demarcated, irregular, yellowish-grey nodule, 7 x 5 x 4 cm. in size, was present in the left costophrenic angle. Microscopically this was a well-differentiated squamous cell carcinoma filling the alveoli but not involving the alveolar septa. Bronchial involvement could not be demonstrated. The hilar nodes were free from malignant involvement.

Incidental findings were moderately widespread arteriosclerosis, a remote, small fibrous scar at the apex and anterior wall of the left ventricle of the heart; multiple cortical adenomata of the kidneys; benign prostatic hyperplasia and leukoplakia of the esophagus. No other sites of carcinomatous involvement could be found.

In summary, this was apparently a case of adenocarcinoma of the stomach with massive hepatic metastases and an incidental squamous cell carcinoma of the lung.

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## SPECIAL STUDIES

The first sign of the existence of an unusual condition was the difficulty encountered when a routine white blood cell count was attempted. On diluting the blood with reagent (dilute acetic acid), immediate clotting of the blood occurred, so that it was impossible to suspend the white cells for counting. It was readily shown that this phenomenon was a characteristic feature of the serum or plasma, and the clot could be produced by adding 3% acetic acid to the patient's serum or plasma (Fig. 1). The behaviour of the serum in this case suggested that the substance producing the clot might be either hyaluronic acid or a mucin, as these substances characteristically form a similar clot

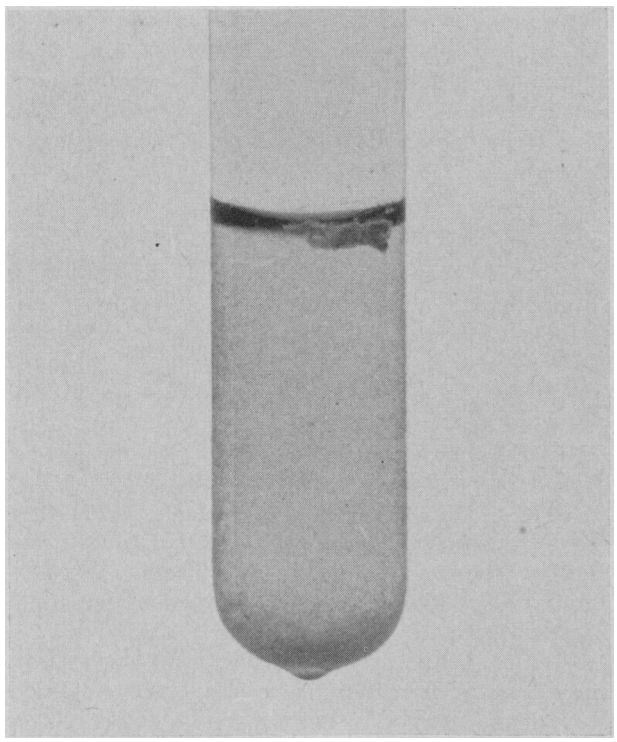

Fig. 1.—Mucinoid clot produced by addition of 3% acetic acid to the patient's serum.

with dilute acetic acid. The presence of hyaluronic acid was ruled out because the clot gave a strongly positive biuret reaction, and incubation of serum with hyaluronidase did not affect the subsequent appearance of the clot when acetic acid was added.

A quantity of the clot was prepared from serum obtained post mortem, washed with dilute acetic acid and then acetone, powdered and dried. A weighed quantity of the powder was dissolved with difficulty in 0.1N sodium hydroxide. Chemical analysis[2] revealed that this material contained the following constituents: nitrogen (Kjeldahl), 12%; protein (biuret), 55%; hexose,[2] 7.1%; hexosamine, 1.8%; sialic acid, 5.4%; and fucose, 0.8%. No lipid was extractable. The chemical composition of the precipitate therefore approximates that of a mucin. Its concentration in the serum was about 0.7%; i.e. roughly 12% of the serum protein consisted of this mucin.

## DISCUSSION

A review of the literature has not revealed any report of a similar case. Two thousand consecutive sera appearing in the laboratory were tested with dilute acetic acid, but no further example of this type of protein was discovered. An acid-precipitable globulin has been described by Greenspan,[1] but this was quite different from the mucin present in the serum of the patient described in this report. In our case, after removal of the mucin with acetic acid, Greenspan's acid-precipitable globulin could be demonstrated in the serum.

It is presumed that the tumour in the liver was able, in some way, to secrete its mucin into the blood, where it circulated. Presumably the finding of this phenomenon in another case might lead one to suspect a similar pathologic condition. The presence of this peculiar mucin might be recognized during the performance of a routine white blood cell count.

## SUMMARY

A case report is presented concerning a 72-year-old man with an adenocarcinoma of the stomach with hepatic metastases, whose circulating blood contained a protein which coagulated on acidification with dilute acetic acid, and which was first detected during the course of a routine white blood cell count. The chemical composition of the coagulated protein was that of a mucin. No similar case report has been found in the literature.

## REFERENCES

1. GREENSPAN, E. M.: *J. Mt. Sinai Hosp. N.Y.*, 21: 279, 1955.
2. GOTTSCHALK, A.: The chemistry and biology of sialic acids and related substances, Cambridge University Press, London, 1960.

## PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

Alberta is again proving itself to be a most valuable laboratory for experiments in legislation, and with the courage of youth it does not count the cost of the service which it is rendering. The most recent experiment which it has undertaken is in the field of medicine. On December 20th, assent was obtained to an amendment of the "Medical Profession Act," giving sanction to principles and practices which have been successfully resisted in all other parts of the world.

The medical council is enjoined to admit upon the register the name of any person who can produce a certificate from the registrar of the University of Alberta that he is qualified to practise osteopathy or homoeopathy, and the examination of candidates is to be undertaken by the university. It is expressly provided, also, that the approval of the college of physicians and surgeons shall not apply to the subjects in which osteopaths and homoeopaths shall be examined.

Section nine is perhaps the most interesting part of the experiment. It provides that any person who has practised osteopathy in Alberta for at least four months previous to the passing of the Act shall be granted a certificate without examination.—*Canad. Med. Ass. J.*, 2: 139, 1912.